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DEBERRY, REGINA M	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Mail 4-20-04

Application Number: 09/606,569
Filing Date: June 29, 2000
Appellant(s): Bigazzi

Peter James Franco
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 17 November 2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The Appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The Appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1-5 stand or fall together because Appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

6,086,898	DeKruyff *et al.*	(Reference cited by Appellant in amendment filed 23 April 2003)

Bani *et al.*, 1997, Endocrinology Vol. 138/5:1909-1915.

Masini *et al.*, 1995, Inflammation Research 44 (Suppl. 1) S12-S13.

Piccinni *et al.*, Annals of the New York Academy of Sciences. Neuroimmunomodulation 917:844-852 (2000). Paper presented at the 4th International Congress of the International Society for Neuroimmunomodulation, Sept. 29-Oct. 2, 1999.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 U.S.C. § 103

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bani *et al.* (Endocrinology 138/5: 1909-1915, 1997) in view of Masini *et al.* (Abstract, Inflammation Research 44 (Suppl. 1) S12-S13, 1995).

The instant claims are drawn to:

a method of treating a Th2 dominated disease in a human patient exhibiting said disease, comprising administering to the patient an effective amount of relaxin or derivative thereof for relieving said disease,

a method of inhibiting a pathogenic Th2 response in a human patient exhibiting said pathogenic Th2 response, comprising administering to the patient an effective amount of relaxin or derivative thereof for inducing endogenous IFN-γ production for inhibiting said pathogenic Th2 response,

a method of stimulating the development of activated human T cells into Th1-like effectors for treating a Th2 dominated disease in a human patient exhibiting said

disease, comprising administering to the patient an effective amount of relaxin or derivative thereof for stimulating said development,

a method of treating a Th2 dominated disease in a human patient exhibiting said disease, comprising administering to the patient an effective amount of relaxin or derivative thereof for enhancing Th1 response of the immunological system of the patient for relieving said disease,

and a method of treating a Th2 dominated disease in a human patient exhibiting said disease, comprising administering to the patient an effective amount of relaxin or derivative thereof for inducing endogenous IFN-γ production for relieving said disease.

Bani *et al.* teach that relaxin (RLX) counteracts the respiratory and histopathological abnormalities of an experimentally induced asthma-like reaction in guinea pigs. Bani *et al.* state that the ability of RLX to stimulate the production of nitric oxide (NO) by mast cells and platelets, further strengthens the hypothesis of a beneficial action of RLX in asthma, as nitric oxide has been shown to cause relaxation of lung airways and blood vessels and improve asthmatic symptoms and favor lung perfusion. Bani *et al.* teach that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans (Introduction). Thus the guinea pig is being employed as an animal model for asthma (Emphasis added). Bani *et al.* state that the results obtained from the current study show that RLX counteracts the respiratory and histopathological abnormalities of an

experimentally induced asthma-like reaction in guinea pig. Bani *et al.* teach that RLX causes a marked reduction of the recruitment of leukocytes in the lungs (Discussion).

Furthermore, asthma is a Th2 dominated disease, which elicits a pathogenic Th2 response. The treatment of a Th2 dominated disease or the inhibition of a pathogenic Th2 response will occur by enhancing a Th1 response. IFN gamma is induced in a Th1 response. Asthma is being treated with RLX. Therefore, the Th1/Th2 responses will inherently occur in a subject treated with RLX. The functional properties/characteristics of RLX will naturally cause these responses.

Masini *et al.* teach that RLX inhibits histamine release from isolated rat serosal mast cells. Neither Bani *et al.* or Masini *et al.* teach the administration of RLX in humans.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Bani *et al.* regarding the administration of RLX to guinea pigs to treat asthma-like reactions, because Bani *et al.* teach that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans. The motivation and expected success is provided by Bani *et al.*, who demonstrate that allergic asthma in guinea pigs can be treated with RLX. Also, Masini discloses the possibility that RLX or RLX derived drugs may be used in the future for the clinical management of allergic diseases (page S13). Bani *et al.* state that the study provides evidence for an anti-asthmatic property of RLX and raises the possibility of new therapeutic strategies for allergic asthma in humans

using RLX (abstract). In addition, Bani and Masini both disclose that RLX may be used in therapeutics to treat allergic conditions.

(11) Response to Argument

Appellant summarizes the experiments of Masini *et al.* (1995, Inflammation Research 44 (Suppl. 1) S12-S13) and Bani *et al.* (1997, Endocrinology 138/5:1909-1915)(p. 5, last paragraph through p. 7 of the Brief). Appellant states that despite the Masini conclusion that the rat cell based dependency of RLX-induced vasodilation on NO production raises the possibility that RLX or RLX-derived drugs may be used to treat allergic and peripheral vascular diseases, the Bani finding that RLX reduces respiratory abnormalities in guinea pigs, promotes dilation of alveolar blood capillaries and reduces the thickness of the air-blood barrier thereby providing evidence for an anti-asthmatic property of RLX, still only leads Bani to regard the results as raising the possibility of new therapeutic strategies for allergic asthma in humans (p. 7, last paragraph). Appellant argues that given the concept that asthma is a species of a Th2 dominated disease genus, it is clear that the instant invention concerns treating asthma in human beings, not in rats (Masini) or guinea pigs (Bani) (p. 8 of the Brief).

The Examiner understands that Appellant is arguing the validity of the results of Masini and Bani because those experiments were employed in animals and not human beings. Appellant's arguments have been fully considered but are not found to be persuasive because Bani *et al.* state that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte

infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans. Bani *et al.* are using a well-established animal model for asthma in humans.

Appellant maintains that Masini only indicates that RLX acts by causing endogenous NO production to inhibit histamine release, in rat cell based test, and it is only on the basis of NO production that RLX is thought to raise the possibility of use to treat allergic diseases (p. 8, second paragraph). Appellant states that such Masini assertion is not motivation to carry out the present invention with an expectation of success, but rather a speculative invitation to experiment in the empirical and unpredictable medical arts. Appellant argues that Bani only shows that RLX has an anti-asthmatic property in treating ovalbumin pre-sensitized guinea pigs, similarly to Masini by endogenous production of NO which has been shown to exert beneficial effects on asthma and thus likewise it is mainly on the basis of NO production that RLX is thought to raise the possibility of use to treat asthma. Appellant maintains that nothing is said in Masini and/or Bani that teaches that RLX is useful to treat asthma in human beings. Appellant states that at best, despite any Examiner asserted art-based motivation to the skilled artisan to combine these two references, Masini and Bani present the classic situation that in view of the suggested use of RLX to treat allergic diseases (Masini) and to counteract allergic asthma in guinea pigs (Bani), expressly thought in each of these two references to involve endogenous NO production, it would be obvious to try use of RLX to treat asthma with respect to human beings. Appellant states that an invention must be obvious over the art per se, in the sense of 35 USC 103, without having to try in

order to determine whether the result is successful or unsuccessful. Appellant contends that there is no art taught equivalency between rat and/or guinea pig based RLX experiments and human based RLX experiments in general, or in particular regard to endogenous NO production, on the one hand, and TH1 cell production as opposed to Th2 cell production, on the other hand (p. 9, first paragraph).

The Examiner understands that Appellant is arguing that that there is no art taught equivalency between rat and/or guinea pig based RLX experiments and human based RLX experiments in general and that there was no motivation to carry out the present invention with an expectation of success. The Examiner understands that Appellant is arguing that it is only on the basis of NO production that RLX is thought to raise the possibility of use to treat allergic diseases. Appellant's arguments have been fully considered but are not found to be persuasive. Bani *et al.* state that, "it has been established that the release of IgE-dependent mediators from inflammatory cells, namely granule-associated mast cell mediators (histamine, eosinophil and neutrophil chemotactic factors) and membrane-derived agents from activated mast cells, platelets and macrophages (leukotrines, PGs and platelet-activating factors) play a major role in the pathogenesis of allergic asthma" (Introduction, Emphasis added). Masini *et al.* teach that "RLX inhibits secretagogue-stimulated histamine release" by isolated rat serosal mast cells and "prevents mast cell degranulation" induced by calcium ionophore in rat mesenteric mast cells *in vivo* (page S13). Thus both references teach that RLX inhibits specific IgE-dependent mediators known to play a major role in the pathogenesis of allergic asthma. Appellant maintains that nothing is said in Masini and/or Bani that

teaches that RLX is useful to treat asthma in human beings. However, Bani *et al.* clearly state that their study "provides evidence for an anti-asthmatic property of RLX and raises the possibility of new therapeutics strategies for allergic asthma in humans" (Abstract). Masini *et al.* state that, "RLX or RLX-derived drugs may be used in the future for the clinical management of allergic and peripheral vascular diseases" (page S13, last paragraph). Furthermore, 35 U.S.C. 103(a), which forms the basis for all obviousness rejections, states a patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. The subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. The motivation and expected success is provided by Bani *et al.*, who demonstrate that allergic asthma in guinea pigs can be treated with RLX. Both Bani and Masini disclose that RLX may be used for the clinical management of allergic diseases and new strategies for allergic asthma in humans. Furthermore, Bani *et al.* state that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans (animal model for asthma in humans).

Appellant asserts that the applied art is based on efforts of appellant herein with co-authors and any personal knowledge of appellant herein may not be imputed to the

art (p. 9, second paragraph of the Brief). Appellant contends that it is clear from Masini and Bani that the various co-authors therein in reality represent the skilled artisan in this field of endeavor, i.e. the unpredictable medical arts, where empirical tests are required to establish useful advances, and where speculation as to mechanisms of action or possible medical uses cannot be accepted place of empirical test results. Appellant asserts that these co-authors as skilled artisan do not say that rat derived cell tests (Masini) and guinea pig tests (Bani) teach that RLX is useful to treat asthma in human beings, but rather that the Masini test results of rat cell based dependency of RLX-induced vasodilation on NO production raises the possibility that RLX or RLX-derived drugs may be used to treat allergic and peripheral vascular diseases, and likewise that the Bani guinea pig test results that RLX reduces respiratory abnormalities and promotes dilation of alveolar blood capillaries and reduces the thickness of the air-blood barrier, provides evidence for an anti-asthmatic property of RLX, thus similarly raising the possibility of new therapeutic strategies for allergic asthma in humans. Appellant argues that there is no art basis to equate guinea pig based tests as used in Bani, with human cell based tests as used herein (p. 10, first paragraph of the Brief). Appellants states that both Bani and Masini constitute the work of individuals who comprise skilled artisans in the unpredictable empirical medical field, and who do not state, as the Examiner implies, that guinea pig based tests are equivalent to human cell based tests. Appellant argues that Bani and Masini both premise their results on endogenous NO production, which only raises the possibility that RLX may be useful or may not be useful for treating human beings.

Appellant's arguments have been fully considered but are not found to be persuasive because Appellant fails to acknowledge the merit of animal models. It is well known to those skilled in the art that experimental treatments employed in animal models always proceed those treatments in human beings. Appellant argues that there is no art basis to equate guinea pig based tests as used in Bani, with human cell based tests as used herein, but Bani *et al.* state that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans. Thus the guinea pig is being employed as an animal model for asthma. The Examiner agrees with Appellant that Bani and Masini are skilled artisans. Thus, Bani and Masini do not speculate as to mechanisms of action or disclose dubious results in the cited references. Both inventors disclosed that RLX may be used for the clinical management of allergic diseases and new strategies for allergic asthma in humans. Furthermore, when relying on a combination of two or more references to establish a prima facie case of obviousness, the PTO must show that there is some suggestion or motivation to combine the prior art references. This suggestion or motivation can be found in the prior art references themselves, in the knowledge generally available to one skilled in the art or, in some cases, from the nature of the problem to be solved. Bani and Masini provided motivation when they both disclosed that RLX may be used for the clinical management of allergic diseases and new strategies for allergic asthma in humans. One skilled in the art would accept a positive

result in an animal models (guinea pig of Bani *et al.*) as motivation and expected success to proceed with treatments in human beings.

Appellant states that the Examiner's assertion that the mechanism by which you get relief of disease is not relevant because it inherently happens, is not well take (bottom of p. 10 of the Brief). Appellant states that it is only because of the Bani and Masini proposed RLX-induced endogenous NO production mechanism of action explanation that the possibility is raised that RLX may be useful to treat human beings, not because of the mechanism of action effect of RLX on any Th2 dominated disease as found per the present invention (top of p. 11 of the Brief). Appellant states that this is not a case where the art shows that human cell based tests indicate that endogenous NO production is found and on the basis of which the possibility is raised that RLX may be useful to treat human beings. Appellant states it is certainly not the case where the art shows that human cell based tests indicate asthma to be a Th2 dominated disease and that it is treatable in human patients by RLX (claim 1), or that a pathogenic Th2 response is inhibitable in human patients by RLX to induce endogenous IFN-gamma production (claim 2), or that development of activated human T cells into Th1-like effectors is stimulatable by RLX to treat a Th2 dominated disease in human patients (claim 3) or that a Th2 dominated disease is treatable in human patients by RLX to enhance the Th1 response of the immunological system (claim 4) or that a Th2 dominated disease is treatable in human patients by RLX to induce endogenous IFN gamma production (claim 5). Appellant maintains that such is the basis of the present invention.

The Examiner understands that, Appellant is arguing that the Bani and Masini references does not teach those experiments in humans. The Examiner understands that Appellant is arguing that that there is no art taught equivalency between rat and/or guinea pig based RLX experiments and human based RLX experiments in general and that there was no motivation to carry out the present invention with an expectation of success. The Examiner understands that Appellant is arguing that the art does not show that human cell based tests indicate asthma to be a Th2 dominated disease. The Examiner understands that Appellant is arguing that Bani and Masini proposed RLX-induced endogenous NO production mechanism of action explanation that the possibility is raised that RLX may be useful to treat human beings, does not correlate to the mechanism of action effect of RLX on a Th2 dominated disease, a pathogenic Th2 response, induction of endogenous IFN gamma production or enhancement of the Th1 response of the immunological system as found per the present invention.

Appellant's arguments have been fully considered but are not found to be persuasive because as was stated above, it is well known to those skilled in the art that experimental treatments employed in animal models always proceed treatments in human beings. Bani *et al.* state that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans. Bani *et al.* teach that RLX counteracts the respiratory and histopathological abnormalities of an experimentally induced asthma-like reaction in guinea pigs. Bani *et al.* state that the ability of RLX to stimulate the production of nitric oxide (NO) by mast

cells and platelets further strengthens the hypothesis of a beneficial action of RLX in asthma, as nitric oxide has been shown to cause relaxation of lung airways and blood vessels and improve asthmatic symptoms and favor lung perfusion. Bani *et al.* demonstrate that allergic asthma in guinea pigs can be treated with RLX. Bani and Masini both disclose that RLX may be used in therapeutics to treat allergic conditions.

In addition, DeKruyff *et al.*, US Patent No. 6,086,898 (reference cited by Appellant in an amendment filed 23 April 2003) teach methods of converting a Th2 type allergic immune response into a Th1 type immune response. DeKruyff *et al.* teach that production of IL-2 and IFN during Th1 dominated response is associated with vigorous cell mediated immunity, the induction of IgG2a and inhibition of IgE synthesis, and with resistance to intracellular pathogens. The production of IL-4, IL-5 and IL-10 during Th2 dominated response is associated with humoral immunity and protection from autoimmune pathology. DeKruyff *et al.* teach that overexpression of Th2 cytokines by allergen specific CD4+T cells can result in the development of allergic disease and asthma (column 1, lines 52-61). DeKruyff *et al.* teach methods for the treatment of allergic and other immune disorders associated with overproduction of Th2 type cytokines by antigen specific T cell cells. These methods are useful in converting an established antigen specific Th2 type T cell response to a Th1 type immune response. Conditions of particular interest include allergic conditions associated with the production of Th2 cytokines and/or IgE antibodies including asthma (column 3, lines 14-30), DeKruyff *et al.* state that one useful application of the invention is in the treatment of asthma. DeKruyff *et al.* employ the use of heat killed Listeria

monocytogenes (HKL) as an adjuvant to reverse antigen specific Th2 dominated response, shifting the reaction to a Th1 type response in asthma (column 4, lines 19-51). DeKruyff *et al.* state that HKL as an adjuvant dramatically decreases the effects of asthma.

Thus, from the DeKruyff *et al.* reference, it is taught that a Th2 dominated disease, a pathogenic Th2 response, the development of activated human T cells into Th1-like effectors for treating a Th2 dominated disease, enhancing Th1 response and induction of endogenous IFN gamma production are all inter-related. The treatment of a Th2 dominated disease or the inhibition of a pathogenic Th2 response can occur by enhancing a Th1 response. IFN gamma is induced in a Th1 response. Asthma is a Th2 dominated disease, which elicits a pathogenic Th2 response. Bani and Masini teach the administration of RLX to treat asthma (a Th2 dominated disease which elicits a pathogenic Th2 response). Thus Bani and Masini teach a method of treating a Th2 dominated disease and a method for inhibiting a pathogenic Th2 response comprising administering RLX (in animal models). Thus if RLX can treat a Th2 dominated disease/inhibit a pathogenic Th2 response (i.e. asthma), it must have the functional characteristics and/or properties to develop activated human T cells into Th1-like effectors, enhance a Th1 response, and induce endogenous IFN gamma production. The instant claims are drawn to the use of a known protein, wherein the use recites the function and characteristic of the protein. The instant claims recite the inherent results of treatment with RLX (Emphasis added).

Appellant states that as noted in Cronin (US Patent 5,166,191), cited in Appellant's Bigazzi-296, RLX is difficult to recover in pure form, being generally obtained as a crude aqueous extract from sow corpora lutea, and was only recently obtained as highly purified RLX from the ovaries of pregnant pigs, rats, shark, and the placentas of horses and rabbits, with partially purified RLX being obtained from cow and human corpora lutea, placentas, and decidua (bottom of p. 12 of the Brief). Appellant cites column 2, lines 15-35. Appellant summarizes the background art section of Cronin *et al.*, US Patent 5,166,191. Appellant states that Cronin notes that the structure of RLX has apparently diverged considerably among species during evolution. Appellant states that Cronin emphasizes the unpredictability as to medical uses of RLX in regard to various therapies there discussed, as the confusing results as to given medical uses that have been obtained therewith.

The Examiner understands that Appellant is arguing that the human RLX preparations were demonstrated to be difficult to obtain in pure form and that there is unpredictability as to the medical uses of RLX in regard to various therapies. Appellant's arguments have been fully considered but are not found to be persuasive. Cronin *et al.* teach that two human gene forms of RLX have been identified by genomic cloning. Cronin cites the dates of the papers which published the human genes of RLX (1981 and 1982). In addition, two US Patents 4,758,516 and 4,871,670 (issued 1988 and 1989 respectively) teach the human gene forms of RLX. The human gene form of RLX has been known for over twenty years. Thus, the RLX protein does not have to be purified from different sources, the protein can made recombinantly. Cronin states that

the art designated definition of "RLX" generally including polypeptides comprising the amino acid sequence of a naturally occurring (human or non-human animal) RLX. Therefore, "RLX" encompasses all species. Furthermore, the instant claims are drawn to RLX. Neither Cronin nor the instant specification differentiates between methods using different species of RLX. Cronin *et al.* disclose reports on the effect of RLX administration on blood vessels and blood pressure. Cronin *et al.* state in view of these contradictory finding, the effect of RLX on arterial pressure is at best unclear (column 5, lines 1-2). The instant claims are drawn to methods of treating Th2 dominated diseases not blood pressure. Furthermore, the objection is based on the level of skill in the art at the time the invention was made. The Cronin *et al.* patent issued in 1992, therefore the majority of the references used in the background art dates back to the early nineties and/or late eighties. It is unclear to the Examiner how this is applicable to the argument at hand because the Bani and Masini references clearly teach the efficacy of RLX in the treatment asthma and allergic conditions.

Appellant states that Bigazzi-296, like Cronin, also confirm that the structure of RLX, is different for each species of animals and has been difficult to obtain in pure form, limiting the value of medical use test results and therewith and emphasizing the unpredictability of its therapeutic use due to its dose-dependency (bottom of p. 14 of the Brief). Appellant states that there is no art supported basis for concluding that tests on animal derived cells such as guinea pig derived cells Bani or rat derived cells per Masini are equivalent to human derived cells, or that test using RLX in a cellular environment (animal subjects) are acceptable to establish predictably corresponding use in another

cellular environment (human patients) (top of p. 15 of the Brief). Appellant argues that Bani and Masini are not concerned with the instant methods. Appellant maintains that any motivation of the skilled artisan to combine Bani and Masini would still result only in speculative raising of the possibility that RLX could be used to treat allergic disease (Masini) or asthma (Bani) in human beings. Appellant asserts that this is far different from the Examiner's unsupported position that the combination of Bani and Masini teaches in fact that it is obvious in the sense of 35 USC 103 that RLX is usable to treat asthma in human beings. Appellant states that this unsupported position of obviousness on the part of the Examiner could only occur by impermissible hindsight use of the instant invention itself to show that it is not an invention. Appellant states that appellant was first to recognize RLX use in humans to treat Th2 dominated diseases based on appellant's recognition that RLX has an inhibiting effect on pathogenic Th2 response (top of p. 16 of the Brief). Appellant states that Bani and Masini have not enriched the medical arts by providing a new method of treating a Th2 dominated disease or pathogenic Th2 response in a human patient, but rather at best alone or in combination present a speculative invitation to experiment to see whether the raised possibility that RLX may be able to treat asthma in human beings is actually correct or incorrect. Appellant maintains that the invention herein has enriched the medical arts by providing a new and unobvious therapeutic method empirically useful for treating human patients. Appellant argues that Bani and Masini are not concerned with the instant methods of treating a Th2 dominated disease in a human patient, inhibiting a

pathogenic Th2 response in a human patient or stimulating the development of activated human T cells into Th1-like effectors in a human patient.

Appellant's arguments have been considered but are not deemed persuasive. As was stated above, Cronin *et al.* cites the unpredictability of RLX therapeutics in methods involving blood vessels and blood pressure not methods of treating Th2 dominated diseases. The sections cited by Appellant for Bigazzi *et al.* state that the physiological significance of these observations remained obscure and up to now it was not known whether or not RLX influences the *circulatory system*. The cited sections are not applicable to the argument at hand as the Bani and Masini references teach the efficacy of RLX in the treatment asthma and allergic conditions. As was stated above, the human gene form of RLX has been known for over twenty years, thus the protein can be made recombinantly. The instant claims are drawn to RLX. Neither Bigazzi or Cronin differentiates between the use of different species of RLX. Contrary to Appellant's assertion, the Examiner's position of obviousness did not occur by impermissible hindsight use of the instant invention itself to show that it is not an invention because Bani and Masini both administer RLX to treat a Th2 dominated disease. The species (asthma) correctly anticipates the claimed genus (Th2 dominated disease, pathogenic Th2 response). The Bani and Masini references teach the species of what is broadly claimed (method of treating a Th2 dominated disease, method of inhibiting a pathogenic Th2 response). The Bani and Masini references teach the exact same method step (administering RLX in a subject exhibiting a Th2 dominant disease or exhibiting a pathogenic Th2 response). The only difference, is the instant claims are drawn to

humans. However the guinea pig of Bani *et al.* is a proper model because repeated exposure to antigen cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans.

As was stated earlier, Appellant fails to acknowledge the merit of animal models. Bani *et al.* teach that in the guinea pig, repeated exposure to antigen has been demonstrated to cause airway hyper-responsiveness and leukocyte infiltration of lung tissue mimicking histological and pharmacological correlates of asthma in humans. One skilled in the art would accept a positive result in an animal model (guinea pig of Bani *et al.*) as motivation and expected success to proceed with treatments in human beings. The guinea pig is being employed as an animal model for asthma. Bani and Masini provided motivation when they both disclosed that RLX may be used for the clinical management of allergic diseases and new strategies for allergic asthma in humans.

It is unclear to the Examiner why Appellant thinks that Bani and Masini would be trying to treat asthma in a guinea pig or in a rat (Emphasis added). Bani and Masini are clearly concerned with treatments in humans. Bani and Masini both disclose that RLX may be used in therapeutics to treat allergic conditions or asthma. The species (asthma) anticipates the claimed genus (Th2 dominated disease, pathogenic Th2 response). As was stated above, asthma is a Th2 dominated disease and elicits a pathogenic Th2 response. The treatment of a Th2 dominated disease or the inhibition of a pathogenic Th2 response will occur by enhancing a Th1 response. IFN gamma is

induced in a Th1 response. The instant invention is drawn to the use of a known protein wherein the use recites the function and characteristic of the protein.

Appellant cites In re Tomlinson *et al.*, 150 USPQ 623, 626 (1966) (bottom of p. 16 of the Brief). Appellant states that the art rejection under 35 USC 103 is unwarranted since it is based on impermissible hindsight inclusion of the instant disclosure to show that the instant invention is not an invention and an implicit holding that on the basis of Bani and Masini it would be obvious to try experiments (p. 18 of the Brief). Appellant cites the specification page 14, lines 1-12. Appellant states that the artisan would be motivated to experiment, to ascertain whether or not RLX is useful to treat asthma in human subjects.

Appellant's arguments have been fully considered but are not deemed persuasive. As was state above, the Examiner's position of obviousness did not occur by impermissible hindsight use of the instant invention itself to show that it is not an invention. The DeKruyff *et al.* reference teaches that a Th2 dominated disease, a pathogenic Th2 response, the development of activated human T cells into Th1-like effectors for treating a Th2 dominated disease, enhancing Th1 response and induction of endogenous IFN gamma production are all inter-related. The treatment of a Th2 dominated disease or the inhibition of a pathogenic Th2 response can occur by enhancing a Th1 response. DeKruyff *et al.* teach that overexpression of Th2 cytokines by allergen specific CD4+T cells result in the development of allergic disease and asthma. A Th1 response will induce IFN gamma production. The Bani and Masini references teach the administration of RLX to treat asthma (a Th2 dominated diseases

which elicits a pathogenic response). The instant claims are drawn to the use of a known protein, wherein the use recites the function and characteristic of the protein. The instant claims recite the inherent results of treatment with RLX. Contrary to Appellant's assertion, the teachings of Bani and Masini are not "efforts to attempt or try". Experiments of treatment do not *start* in human beings. Experimental treatments in animal models precede those treatments in human beings. One skilled in the art would accept a positive result in an animal models (guinea pig of Bani *et al.*) as motivation and expected success to proceed with treatments in human beings.

Therefore, for reasons set forth above, Appellants arguments and exhibits have been fully and carefully considered, but are not considered sufficient to rebut the case of 35 U.S.C. 103(a) obviousness and it is believed that the rejections should be sustained.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

RMD
April 6, 2004

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